

BOMBESIN RECEPTOR SUBTYPES IN THE CNS AND GLIOBLASTOMA CELLS. Terry W. Moody and James F. Battery, Dept. Biochem. and Molecular Biology, George Washington Univ. Med. Ctr., Washington, D.C. 20037 and Lab. Biol. Chem., NCI, Bethesda, MD 20892.

Two types of bombesin (BN) receptor subtypes include gastrin releasing peptide (GRP) and neuromedin B (NMB). Both receptors have 7 transmembrane domains and interact with guanine nucleotide binding proteins. GRP receptors (GRPR) bind BN and GRP but not NMB with high affinity and interact with antagonists such as (D-Phe⁶)BN⁶⁻¹³methyleneester and (Psi^{13,14}, Leu¹⁴)BN (Psi-13,14). NMB receptors (NMBR) bind NMB but not GRP with high affinity and interact with the substance P antagonist (D-Arg¹, D-Pro², D-Trp^{7,9}, Leu¹¹)substance P ((APTTL)SP). Using in vitro autoradiographic techniques and in situ hybridization techniques, high densities of GRPR but not NMBR were found in the paraventricular hypothalamic nucleus and nucleus accumbens (Moody, Wada and Battery, In "Handbook of Chemical Anatomy," A. Bjorklund, T. Hokfelt and M.J. Kuhar (Eds) 55-95 (1992)). In contrast, high densities of NMBR but not GRPR were found in the anterior olfactory nucleus and central medial thalamic nucleus. Moderate densities of GRPR and NMBR were present in the cortex, amygdala, hippocampus, nucleus tractus solitarius and dorsal horn of the spinal cord. By immunocytochemistry and in situ hybridization, high densities of GRP are present in the paraventricular hypothalamic nucleus, cortex, hippocampus and amygdala whereas NMB is present in the olfactory bulb and dentate gyrus. Therefore the CNS distribution of GRP and NMB and its receptors are unique.

The second messengers used by GRP and NMB were investigated. GRP and NMB stimulate phosphatidylinositol turnover. In human glioblastoma cell line U-118 or U-138, GRP caused a transient elevation of cytosolic Ca²⁺ from 150 to 300 nM and the increase caused by GRP was blocked by Psi-13,14. In C6 rat glioma cells NMB elevates the cytosolic Ca²⁺ and (APTTL)SP inhibits the increase caused by NMB. Also, NMB stimulates the growth of C6 cells and the growth is inhibited by (APTTL)SP. These data suggest that the signal transduction mechanisms for GRP and NMB are similar.